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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,376	06/18/2001	John Peter Morseman	31676.0248	6731

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EXAMINER

COUNTS, GARY W

ART UNIT PAPER NUMBER

1641

DATE MAILED: 07/15/2003

(9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/882,376

Applicant(s)

MORSEMAN ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 1 and 2 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 December 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 & 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the elected invention concerns time resolved fluorescence energy transfer from a donor fluorophore to an allophycocyanin fluorophore prepared in a particular way. The energy transfer between fluorophores is not directly detectable, and therefore is measured indirectly, either by detecting the facilitation of donor absorbance by transfer of energy to the acceptor fluorophore or by measuring fluorescence from the acceptor fluorophore as a result of the energy transfer and thus, the present invention provides equivalent enhancement of either detection method, and claims 2 and 3 are merely alternative embodiments of the same invention. This is not found persuasive because neither claim nor any other claims is directed solely to the common concept measuring energy absorbed by donor and measuring energy transferred from donor. Claim 2 is directed to measuring energy absorbed by donor compounds whereas Claim 3 is directed to measuring the energy transferred from donor compounds. These are independent concepts involving different materials. The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. The drawings are objected to because there is no Figure 1 present in the application. The drawings begin with Figure 2 and end with Figure 7. It appears that Applicant has deleted Figure 1 or that Figure 1 is missing. The figures should be renumbered appropriately. A proposed drawing correction or corrected drawings are

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required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Applicant is advised that no amendment in an application or the claims can introduce new matter.

Specification

3. The disclosure is objected to because of the following informalities: The Drawings as stated above appear to be missing Figure 1 or either the Drawings were misnumbered. The drawings should be renumbered or missing Figure 1 submitted. The figures need to be renumbered and any reference to the figures in the specification need to be renumbered appropriately to correspond with the renumbered figures (i.e. the Brief Description of the drawings section). In the event a Figure 1 is submitted, appropriate description of Figure 1 would also be required. Appropriate correction is required. Applicant is advised that no amendment in an application or the claims can introduce new matter.

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 11-14 recites distinct donor species. However, on page 9, line 25 – page 10, line 8 in the specification applicant discloses other donor/acceptor pairs. Applicant does not disclose distinct donor species.

Claim Objections

5. Claims 4, 7-11, 13 and 14 are objected to because of the following informalities:
- The claims depend from non-elected claim 2 and should be amended to depend only from elected claim 3. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 7, lines 4-13 in the specification the applicant uses a comparison of 1.5 M sodium perchlorate to 6 M or greater urea or guanidine HCL. The applicant discloses the strongly denaturing chaotropic agents are defined herein as agents having more strongly denaturing effect than 1.5 M sodium percholorate, and preferably as equivalent to 6 M or greater urea or guanidine HCl. Typical denaturants which may be used in this format are sodium percholorate, preferably at concentration about 1 M. The applicant does not disclose other strongly chaotropic agents. There is no description in the specification disclosing other strongly chaotropic agents can be used.

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8. Claims 3-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sodium perchlorate, does not reasonably provide enablement for other strongly chaotropic agents because applicant has no defined a strongly chaotropic agent but rather as disclosed a comparison of 1.5 M sodium perchlorate to 6 M or greater urea or guanidine HCL. . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re Wands* USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a label quantitatively associated with the analyte, the improvement comprising measuring the energy transferred from a donor compounds having the ability to absorb light energy and then transfer this energy to cross-linked allophycocyanin in a time-resolved manner, where the cross-linked allophycocyanin has not been exposed to strongly chaotropic agents after cross-linking.

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The disclosure fails to state or teach one skilled in the art how to select an appropriate chaotropic agent. The specification on page 7, lines 4-13 the applicant uses a comparison of 1.5 M sodium perchlorate to 6 M or greater urea or guanidine HCL. The applicant discloses the strongly denaturing chaotropic agents are defined herein as agents having more strongly denaturing effect than 1.5 M sodium perchlorate, and preferably as equivalent to 6 M or greater urea or guanidine HCl. Typical denaturants which may be used in this format are sodium perchlorate, preferably at concentration about 1 M. However, it does not disclose the use of any other strongly chaotropic agents other than sodium perchlorate. Furthermore, the use of other chaotropic agents on cross-linked allophycocyanin is not well known in the art and thus one of ordinary skill in the art would have a low level of predictability in the art.

The working examples in the specification are limited to the use of 1 M Sodium Perchlorate. Furthermore, applicant does not disclose how long the cross-linked allophycocyanin is subjected to the 1 M Sodium Perchlorate. It is known in the art that exposure time of a protein to a denaturing agent can effect the degree to which the protein is denatured. For instance, a weaker agent can be used but increased exposure time of the agent to the substance can cause it to have the same effect as a stronger agent therefore, it could be considered a strong agent. Because the specification lacks a clear written disclosure for strong chaotropic agents and it is unclear what a strong chaotropic agent is one of ordinary skill would not be able to select an appropriate chaotropic agent. In order to select an appropriate chaotropic agent, one of ordinary

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skill in the art would have to have a high level of predictability in order to successfully select a chaotropic agent without undue experimentation.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 3-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 the recitation "used according to this invention" is vague and indefinite. It is unclear what applicant is trying to encompass. It is recommended to delete this recitation from the claim.

Claim 3 the recitation "having the ability" is vague and indefinite. The recitation is not a positive limitation. It does not constitute a limitation in any patentable sense. Do the donor compounds absorb light energy and then transfer this energy to cross-linked allophycocyanin in a time-resolve manner or not?

Claim 3 "strongly" is vague and indefinite. The term "strongly" is a relative term which renders the claim indefinite. It is unclear what is considered to be a strongly chaotropic agents. Is applicant referring to a specific concentration of the agent which makes it strong or conditions which make it act as a strong chaotropic agent (i.e. a weaker agent can be used but increased exposure time of the agent to the substance can cause it to have the same effect as a stronger agent therefore, it could be considered a strong agent).

Claim 4 "the donor molecule" there is insufficient antecedent basis for this limitation.

Claim 9 the recitation "a ratio of areas" is vague and indefinite. It is unclear what applicant intends.

Claim 9 the recitation "of at least 4" is vague and indefinite. It is unclear what applicant is referring to. At least 4 what?

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 3-6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Homogenous Proximity Tyrosine Kinase Assays, Analytical Biochemistry 269, 94-104 (1999)) in view of Ong et al (Crosslinking of allophycocyanin, Physiol. Veg. 1985, 23 (1), 777-787).

Park et al disclose a method for quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a label quantitatively associated with analyte. Park et al disclose measuring the energy transferred from donor compounds to absorb light energy and then transfer this energy to cross-linked allophycocyanin. Park et al disclose the energy donor can be europium (abstract).

Park et al fail to specifically teach that the cross-linked allophycocyanin has not been exposed to strongly chaotropic agents after cross-linking.

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Ong et al disclose cross-linked agents, which are exposed to 8 M urea after cross-linking. Ong et al disclose that this cross-linked allophycocyanin provides for an allophycocyanin which is stable to dissociation and unaltered in spectroscopic properties and is a valuable reagent for cell sorting, cell analysis and immunoassay.

It would have been obvious to one of ordinary skill in the art to incorporate cross-linked agents such as taught by Ong et al into the method of Park et al because Ong et al teach that this cross-linked allophycocyanin provides for an allophycocyanin which is stable to dissociation and unaltered in spectroscopic properties and is a valuable reagent for cell sorting, cell analysis and immunoassay.

13. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al and Ong et al in view of Applicant's admission of prior art.

See above for teachings of Park et al and Ong et al.

Park et al and Ong et al differ from the instant invention in failing to specifically teach at least two distinct donor species present in different formats.

On page 9, lines 25 – page 10, line 8 in the specification Applicant discloses that the dye of this invention can be used with any known format for FRET. Applicant discloses the known formats. It would have been obvious to one of ordinary skill in the art to incorporate the cross-linked allophycocyanin of Park et al and Ong et al into different well known formats of FRET as disclosed by Applicant for quantitating an analyte by measuring time resolved fluorescence of a label quantitatively associated with the analyte.

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Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Huang et al., (Kinetics of Allophycocyanin's Trimer-Monomer Equilibrium, Biochemistry 1987, 26, 243-245). Huang et al uses sodium perchlorate to dissociate allophycocyanin trimers into monomers.

MacColl (stability of Allophycocyanin's Quaternary Structure, Archives of Biochemistry and Biophysics, Vol. 223, No. 1, May, pp. 24-32, 1983. MacColl teaches the dissociation of allophycocyanin trimers to monomers using chaotropic salts.

MacColl (Phycobiliproteins, CRC Press, 1987, Chapter 4, p. 51-53 and 66, Chapter 6 p. 103) provides general teachings about Allophycocyanin and also teaches allophycocyanin dissociating into monomers.

Kolb et al., Use of Novel Homogeneous Fluorescent Technology in High Throughput Screening, Journal of Biomolecular Screening, Vol. 1, No. 4, 1996. Kolb teach a new fluorescent technology using a cross linked allophycocyanin.

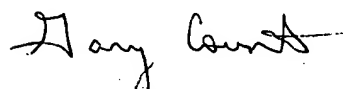
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for

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the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Gary W. Counts
Examiner
Art Unit 1641
July 7, 2003



LONG V. LE
SUPERVISORY PATENT EXAMINER
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07/07/03